RABIES

DISEASE REPORTING

In Washington

Since 1939, only two human cases of rabies have occurred in Washington; one in 1995 and one in 1997.

Bats are the primary reservoir for rabies in Washington State. Bats carrying rabies have been found in almost every county in Washington State. In other parts of the United States, Canada and Mexico, reservoirs include foxes, coyotes, skunks, raccoons, and dogs.

Rabies is almost invariably fatal despite treatment; post-exposure prophylaxis (PEP) should be considered for exposed individuals. Recommendations for post exposure prophylaxis can be found in the section titled: Rabies Post-Exposure Prophylaxis, or by calling DOH Communicable Disease Epidemiology at 1-877-539-4344. A compendium on rabies is available at: http://www.avma.org/resources/default.htm.

Purpose of reporting and surveillance

- To assist in the diagnosis of human and animal cases of rabies.
- To identify contacts of a human rabies case and provide counseling about PEP.
- To facilitate the capture and confinement of potentially rabid animals involved in a human exposure with a defined observation period (dogs, cats, and ferrets); or facilitate histological examination of the brain of potentially rabid animals involved in a human exposure when those animals cannot be observed. This may involve coordination with other agencies, e.g., the Humane Society, animal control, and local law enforcement.

Reporting requirements

- Health care providers: **immediately notifiable**
- Hospitals: **immediately notifiable**
- Laboratories: **immediately notifiable to Local Health Jurisdiction**, specimen submission required
- Local health jurisdictions: notifiable to DOH Communicable Disease Epidemiology within 7 days of case investigation completion or summary information required within 21 days

CASE DEFINITION FOR SURVEILLANCE

Clinical criteria for diagnosis

Rabies is an acute encephalomyelitis that almost always progresses to coma or death within 10 days after the first symptom.

Laboratory criteria for diagnosis

- Detection by direct fluorescent antibody of viral antigens in a clinical specimen (preferably the brain or the nerves surrounding hair follicles in the nape of the neck), or
- Isolation (in cell culture or in a laboratory animal) of rabies virus from saliva, cerebrospinal fluid (CSF), or central nervous system tissue, or
- Identification of a rabies-neutralizing antibody titer ≥5 (complete neutralization) in the serum or CSF of an unvaccinated person.

Laboratory confirmation by all of the above methods is strongly recommended.

Case definition

- Confirmed: a clinically compatible case that is laboratory confirmed.

A. DESCRIPTION

1. Identification

An almost invariably fatal, acute viral encephalomyelitis; onset is often heralded by a sense of apprehension, headache, fever, malaise and indefinite sensory changes often referred to the site of a preceding animal bite. Excitability and aerophobia are frequent symptoms. The disease progresses to paresis or paralysis; spasm of swallowing muscles leads to fear of water (hydrophobia); delirium and convulsions follow. Without medical intervention, the usual duration is 2-6 days, sometimes longer; death is often due to respiratory paralysis.

Diagnosis is made by specific FA staining of brain tissue or by virus isolation in mouse or cell culture systems. Presumptive diagnosis may be made by specific FA staining of frozen skin sections taken from the back of the neck at the hairline. Serologic diagnosis is based on neutralization tests in mice or cell culture.

2. Infectious Agent

Rabies virus, a rhabdovirus of the genus Lyssavirus. All members of the genus are antigenically related, but use of monoclonal antibodies and nucleotide sequencing of the virus demonstrates differences according to the animal species or the geographic location

from which they originate. Rabies related viruses that exist in Africa (Mokola and Duvenhage) have been associated rarely with fatal rabies-like human illness. A new lyssavirus, first identified in 1996 in several species of flying foxes and bats in Australia, has been associated with two human deaths with rabies-like illnesses. This virus has been provisionally named Australian bat lyssavirus. It is closely related to, but not identical to classical rabies virus. Some of the illnesses due to these rabies related viruses may be diagnosed as rabies by the standard FA test.

3. Worldwide Occurrence

Worldwide, with an estimated 35,000-40,000 deaths a year, almost all in developing countries. From 1980 through 1997, in the US, 36 human deaths from rabies have been reported; 12 of these were probably acquired outside the US. Of those who were probably infected within the US, more than half died of bat associated rabies. Since the 1950s human rabies deaths in the US have been gradually decreasing as a result of routine rabies immunization of domestic dogs and cats, and the increasing effectiveness of postexposure prophylaxis regimens.

Rabies is a disease primarily of animals. The only areas currently free of rabies in the animal population include Australia, New Zealand, New Guinea, Japan, Hawaii, Taiwan, Oceania, the UK, Ireland, Iceland, mainland Norway, Sweden, Finland, Portugal, Greece and some of the West Indies and Atlantic islands. Urban (or canine) rabies is transmitted by dogs, whereas sylvatic rabies is a disease of wild carnivores and bats, with sporadic spillover to dogs, cats and livestock. In Europe, fox rabies was widespread, but has decreased since 1978 when oral rabies immunization was begun; in western Europe the number of cases has decreased drastically since 1992, except for bat rabies. Since 1986, bat rabies cases have been reported in Denmark, Holland and West Germany. In the US and Canada, wildlife rabies most commonly involves raccoons, skunks, foxes, coyotes and bats. There has been a progressive epizootic among raccoons in the eastern US for more than a decade, now reaching New England, and currently among coyotes and dogs in south Texas; spread of the virus to domestic animals most frequently involves cats.

4. Reservoir

Many wild and domestic *Canidae*, including dogs, foxes, coyotes, wolves and jackals; also skunks, raccoons, mongooses and other biting mammals. Infected populations of vampire, frugivorous and insectivorous bats are found in Mexico, Central and South America; infected insectivorous bats are found in the US, Canada and now in Europe. In developing countries, dogs remain the principal reservoir. Rabbits, opossums, squirrels, chipmunks, rats and mice are rarely infected, and their bites rarely, if ever, call for rabies prophylaxis.

5. Mode of Transmission

Virus laden saliva of a rabid animal is introduced by a bite or scratch (or, very rarely, into a fresh break in the skin or through intact mucous membranes). Transmission from

person to person is theoretically possible since the saliva of the infected person may contain virus, but this has never been documented. Organ (corneal) transplants taken from persons dying of undiagnosed CNS disease have resulted in rabies in the recipients. Airborne spread has been demonstrated in a cave where myriad of bats were roosting and in laboratory settings, but this occurs very rarely. In Latin America, transmission from infected vampire bats to domestic animals is common. In the US, rabid insectivorous bats rarely transmit rabies to terrestrial animals, wild or domestic.

6. Incubation period

Incubation period-Usually 3-8 weeks, rarely as short as 9 days or as long as 7 years; depends on the severity of the wound, site of the wound in relation to the richness of the nerve supply and its distance from the brain, amount and strain of virus introduced, protection provided by clothing and other factors. Prolonged incubation periods have occurred in prepubertal individuals.

7. Period of communicability

In dogs and cats, usually for 3-7 days before onset of clinical signs (rarely over 4 days) and throughout the course of the disease. Longer periods of excretion before onset of clinical signs (14 days) have been observed with Ethiopian dog rabies strains. In one study, bats shed virus for 12 days before evidence of illness; in another study, skunks shed virus for at least 8 days before onset of clinical signs. Skunks may shed virus for up to 18 days before death.

8. Susceptibility and resistance

All mammals are susceptible to varying degrees, which may be influenced by the virus strain. Humans are more resistant to infection than several animal species; only approximately 40% of untreated Iranians bitten by proven rabid animals developed the disease.

B. METHODS OF CONTROL

1. Preventive measures:

a. Register, license and immunize all dogs in enzootic countries; collect and euthanize ownerless animals and strays. Immunize all cats. Educate pet owners and the public that restrictions for dogs and cats are important (e.g., that pets be leashed in congested areas when not confined on owner's premises; that strange acting or sick animals of any species, domestic or wild, may be dangerous and should not be picked up or handled; that it is necessary to report such animals and animals that have bitten a person or another animal to the police and/or the local health department; that confinement and observation of such animals is a preventive measure against rabies); and that wild animals should not be kept as pets. Where

dog control is sociologically impractical, repetitive total dog population immunization has been effective.

b. Maintain active surveillance for rabies in animals. Laboratory capacity should be developed to perform FA testing on all wild animals involved in human or domestic animal exposures and all domestic animals clinically suspected of having rabies. Educate physicians, veterinarians and animal control officials to obtain/euthanize/test animals involved in human and domestic animal exposures.
c. Detain and clinically observe for 10 days any healthy-appearing ferret, dog or cat known to have bitten a person (unwanted ferrets, dogs and cats may be euthanized immediately and examined for rabies by fluorescent microscopy); ferrets, dogs and cats showing suspicious signs of rabies should be sacrificed and tested for rabies. If the biting animal were infective at the time of the bite, signs of rabies will usually follow within 4-7 days, with a change in behavior and excitability or paralysis, followed by death. All wild mammals that have bitten a person should be sacrificed immediately and the brain examined for evidence of rabies. In the case of bites by a normal behaving, very valuable pet or zoo animal, it may be appropriate to consider postexposure prophylaxis for the human victim, and, instead of sacrificing the animal, hold it in quarantine for 3-12 weeks.
d. Submit immediately to a laboratory the intact heads, packed in ice (not frozen), of animals that die of suspected rabies, for viral antigen testing by FA staining, or, if this is not available, by microscopic examination for Negri bodies, followed by mouse inoculation.
e. Euthanize immediately nonimmunized dogs or cats bitten by known rabid animals; if detention is elected, hold the animal in an approved secure pound or kennel for at least 6 months under veterinary supervision, and immunize against rabies 30 days before release. If previously immunized, reimmunize and detain (leashing and confinement) for at least 45 days.
f. Oral immunization of wildlife animal reservoirs using attenuated or recombinant vector vaccines has been effective in eliminating fox rabies from parts of Europe and Canada. The technique is being evaluated in the US, using air drop of bait containing recombinant vaccine.
g. Cooperative programs with wildlife conservation authorities to reduce fox, skunk, raccoon and other terrestrial wildlife hosts of sylvatic rabies may be used in circumscribed enzootic areas near campsites and areas of human habitation. If such focal depopulation is undertaken, it must be maintained to prevent repopulation from the periphery.
h. Individuals at high risk (e.g., veterinarians, wildlife conservation personnel and park rangers in enzootic or epizootic areas, staff of quarantine kennels, laboratory and field personnel working with rabies, and long term travelers to rabies endemic areas) should receive preexposure immunization. Three types of rabies vaccine are currently available in the US: Human Diploid Cell rabies Vaccine (HDCV), an inactivated vaccine prepared from virus grown in human diploid cell culture; Rabies Vaccine, Adsorbed (RVA), an inactivated vaccine grown in rhesus diploid cells; and Purified Chick Embryo Cell Vaccine (PCEC), an inactivated vaccine grown in primary cultures of chicken fibroblasts. (Other potent cell culture vaccines are available in other countries.) Each vaccine can be given in three 1.0 ml (IM) doses

on days 0, 7 and 21 or 28: This regimen has been so satisfactory that routine postimmunization serologic testing is not routinely recommended but may be advisable for groups at high risk of exposure or immunodeficient persons.

If risk of exposure continues, either single booster doses are given, or preferably serum is tested for neutralizing antibody every 2 years, with booster doses given when indicated. If immunization is given in preparation for travel to a rabies endemic area, 30 or more days should elapse after the 3-dose series before departure; otherwise, the IM regimen should be used. Although immune response has not been evaluated for antimalarials structurally related to chloroquine (e.g., mefloquine, hydroxychloroquine), similar precautions for individuals receiving these drugs should be followed. RVA and PCEC should not be given intradermally.

i. Prevention of rabies after animal bites (postexposure prophylaxis) consists of the following:
    i. Treatment of bite wound: The most effective rabies prevention is immediate and thorough cleaning with soap or detergent and flushing with water all wounds caused by an animal bite or scratch. The wound should not be sutured unless unavoidable for cosmetic or tissue support reasons. Sutures, if required, should be placed after local infiltration of antiserum (see ii, next below); they should be loose and not interfere with free bleeding and drainage.
    ii. Specific immunologic protection: Immunologic prevention of rabies in humans is provided by administration of human rabies immune globulin (HRIG) as soon as possible after exposure to neutralize the virus at the bite wound site, and then by giving vaccine at a different site to elicit active immunity. Only HRIG is licensed in the US, purified equine (ERIG) IG is available in other countries. Animal studies suggest that human disease caused by the Australian bat lyssavirus may be prevented by rabies vaccine and rabies immune globulin, and such post exposure prophylaxis is recommended for persons bitten or scratched by any bat in Australia. In contrast, rabies vaccine is not effective for the treatment of African bat lyssaviruses.

    Passive immunization: HRIG should be used in a single dose of 20 IU/kg; if anatomically feasible, the full dose of HRIG should be infiltrated into and around the bite wound if possible, and the remaining volume given IM at a site distant from vaccine administration. If serum of animal origin is used, an intradermal or subcutaneous test dose should precede its administration to detect allergic sensitivity, and the dose should be increased to a total of 40 IU/kg.

    Vaccine: HDCV, RVA, or PCEC in five 1.0 ml IM doses in the deltoid region; the first as soon as possible after the bite (at the same time as the single dose of HRIG is given), and the other doses 3, 7, 14 and 28-35 days after the first dose. (The intradermal dose/route at multiple sites is being used in several countries for postexposure prophylaxis, but this has not been approved in the US.) In individuals with possible immunodeficiency, a serum specimen should be collected at the time the last dose of vaccine is administered and tested for rabies antibodies. If sensitization reactions appear in the course of immunization, consult health department or infectious

disease consultants for guidance. If the person has had a previous full course of antirabies immunization with an approved vaccine, or had developed neutralizing antibodies after preexposure immunization (see B1h, above) or after a postexposure regimen, only 2 doses of vaccine need to be given-one immediately and one 3 days later. With severe exposure (e.g., head bites), a third dose may be given on day 7. HRIG is not used with this regimen.

iii. The following is a general guide to prophylaxis in different circumstances: If a bite were unprovoked, the animal not apprehended, and rabies present in that species in the area, administer HRIG and vaccine. Bites of wild carnivorous mammals and bats are considered potential rabies exposures unless negated by laboratory tests. If available, the biting animal may be euthanized immediately (with the owner's and health authorities' concurrence) and its brain examined by FA technique to determine whether antirabies treatment is necessary. The decision whether to administer HRIG and vaccine immediately after exposure to dogs and cats or during the observation period (see B1c, above) should be based on the behavior of the animal, the presence of rabies in the area, and the circumstances of the bite. (See Guide, below.)

iv. Immunization with current rabies vaccines carries a very small risk of postimmunization encephalitis; only 2 cases of transient neuroparalytic illness have been reported in the US. Local reactions, such as pain, erythema, swelling or itching at the injection site were reported in 25% of those receiving five 1.0 ml doses. Mild systemic reactions of headache, nausea, muscle aches, abdominal pain and dizziness were reported in about 20%. “Serum sickness-like” reactions, including primarily urticaria with generalized itching and wheezing, were reported infrequently.

However, among those receiving booster doses for preexposure prophylaxis, hypersensitivity reactions occur in approximately 6% of recipients 2-21 days after HDCV, presenting as a generalized pruritic rash, urticaria, possible arthralgia, arthritis, angioedema, nausea, vomiting, fever and malaise. These symptoms have responded to antihistamines; a few have required corticosteroids or epinephrine. Persons exposed to rabies who develop these symptoms should complete the required number of injections but in a setting where reactions can be treated. Systemic allergic reactions in those receiving booster doses of RVA have been rare (reported in less than 1%). No significant reactions have been attributed to HRIG (of human origin); however, antiserum from a nonhuman source produces serum sickness in 5%-40% of recipients. Newer purified animal globulins, in particular equine globulin, have only a 1% risk of reactions. These risks must be weighed against the risk of contracting rabies.

v. Management of animal bites-adapted from the Eighth Report of the WHO Expert Committee on Rabies, 1992 and from the USPHS Advisory Committee on Immunization Practices (MMWR, Rabies Prevention-United States, 1999;48 No. RR-1:January 1999)-should include:

Checklist for Treatment of Animal Bites

1. Clean and flush the wound immediately (first aid).
2. Thorough wound cleansing under medical supervision.
3. Rabies immune globulin and/or vaccine as indicated.
4. Tetanus prophylaxis and antibacterial treatment when required.
5. No sutures or wound closure advised unless unavoidable.

2. Control of patient, contacts and the immediate environment:

a. Report to local health authority.
b. Isolation: Contact isolation for respiratory secretions for duration of the illness.
c. Concurrent disinfection: Of saliva and articles soiled therewith. Although transmission from a patient to attending personnel has not been documented, immediate attendants should be warned of the potential hazard of infection from saliva, and should wear rubber gloves, protective gowns, and protection to avoid exposure from a patient coughing saliva in the attendant's face.
d. Quarantine: None.
e. Immunization of contacts: Contacts who have an open wound or mucous membrane exposure to the patient's saliva should receive antirabies specific treatment (see B1i(ii), above).
f. Investigation of contacts and source of infection: Search for rabid animal and for people and other animals bitten.
g. Specific treatment: For clinical rabies, intensive supportive medical care.

3. Epidemic (epizootic) measures

Applicable only to animals; a sporadic disease in humans.

a. Establish area control under authority of state laws, public health regulations and local ordinances, in cooperation with appropriate wildlife conservation and animal health authorities.
b. Immunize dogs and cats through officially sponsored, intensified mass programs that provide immunizations at temporary and emergency stations. For protection of other domestic animals, approved vaccines appropriate for each animal species must be used.
c. In urban areas of the US and other developed countries, strict enforcement of regulations requiring collection, detention and euthanasia of ownerless and stray dogs, and of nonimmunized dogs found off owners' premises; control of the dog population by castration, spaying or drugs have been effective in breaking transmission cycles.
d. Immunization of wildlife by using baits containing vaccine has successfully contained fox rabies in western Europe and Canada and is in clinical trials in the US; this should prove effective in controlling disease spread in epizootic areas.

4. International measures

a. Strict compliance by common carriers and travelers with national laws and regulations in most rabies free countries or states that require quarantine for 4-6 months. Immunization of animals, certificates of health and origin, or microchip identification of animals may be required.
b. WHO Collaborating Centres.